# Povidone

## 1. Nonproprietary Names

BP: Povidone
PhEur: Polyvidonum
USP: Povidone

## 2. Synonyms

E1201; *Kollidon*; *Plasdone*; poly[1-(2-oxo-1-pyrrolidinyl)ethylene]; polyvidone; polyvinylpyrrolidone; PVP; 1-vinyl-2-pyrrolidinone polymer.

## 3. Chemical Name and CAS Registry Number

1-Ethenyl-2-pyrrolidinone homopolymer
[9003-39-8]

## 4. Empirical Formula Molecular Weight

$(C_6H_9NO)_n$ 2500-3 000 000

The USP XXII (Suppl 9) describes povidone as a synthetic polymer consisting essentially of linear 1-vinyl-2-pyrrolidinone groups, the degree of polymerization of which results in polymers of various molecular weights. It is characterized by its viscosity in aqueous solution, relative to that of water, expressed as a K-value, ranging from 10-120. The K-value is calculated using Fikentscher's equation[1] shown below:

$$\log z = c\left(\frac{75k^2}{1 + 1.5kc}\right) + k$$

where $z$ is the relative viscosity of the solution of concentration $c$, $k$ is the K-value x $10^{-3}$, and $c$ is the concentration in % w/v. Alternatively, the K-value may be determined from the following equation:

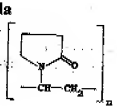
$$K - value = \frac{\sqrt{300c\log z + (c + 1.5c\log z)^2} + 1.5}{0.15c + 0.03c^2}$$

where $z$ is the relative viscosity of the solution of concentration $c$, $k$ is the K-value x $10^{-3}$, and $c$ is the concentration in % w/v. Approximate molecular weights for different povidone grades are shown below:

| K-value | Approximate molecular weight |
|---|---|
| 12 | 2500 |
| 15 | 8000 |
| 17 | 10 000 |
| 25 | 30 000 |
| 30 | 50 000 |
| 60 | 400 000 |
| 90 | 1 000 000 |
| 120 | 3 000 000 |

*See also* Section 8.

## 5. Structural Formula



## 6. Functional Category

Suspending agent; tablet binder.

## 7. Applications in Pharmaceutical Formulation or Technology

Although povidone is used in a variety of pharmaceutical formulations it is primarily used in solid dosage forms. In tableting, povidone solutions are used as binders in wet granulation processes. Povidone is also added to powder blends in the dry form and granulated *in situ* by the addition of water, alcohol or hydroalcoholic solutions. Povidone solutions may also be used as coating agents.

Povidone is additionally used as a suspending, stabilizing or viscosity-increasing agent in a number of topical and oral suspensions and solutions. The solubility of a number of poorly soluble active drugs may be increased by mixing with povidone.

Special grades of pyrogen free povidone are available and have been used in parenteral formulations, *see* Section 14.

| Use | Concentration (%) |
|---|---|
| Carrier for drugs | 10-25 |
| Dispersing agent | up to 5 |
| Eye-drops | 2-10 |
| Suspending agent | up to 5 |
| Tablet binder, tablet diluent, or coating agent | 0.5-5 |

## 8. Description

Povidone is a fine, white to creamy-white colored, odorless or almost odorless, hygroscopic powder. Povidones with K-values equal to or lower than 30 are manufactured by spray-drying and exist as spheres. Povidone K-90 and higher K-value povidones are manufactured by drum drying and exist as plates.

## 9. Pharmacopeial Specifications

| Test | PhEur 1990 | USP XXII (Suppl 9) |
|---|---|---|
| Identification | + | + |
| pH | — | 3.0-7.0 |
| Appearance of solution | + | — |
| Water | ≤ 5.0% | ≤ 5.0% |
| Residue on ignition | — | ≤ 0.1% |
| Sulfated ash | ≤ 0.1% | — |
| Lead | — | ≤ 10 ppm |
| Heavy metals | ≤ 10 ppm | — |
| Aldehydes | ≤ 0.2% | ≤ 0.2% |
| Hydrazine | — | ≤ 1 ppm |
| Vinylpyrrolidinone | ≤ 0.2% | ≤ 0.2% |
| K-value | | |
| ≤ 15 | 85.0-115.0% | 85.0-115.0% |
| >15 | 90.0-108.0% | 90.0-108.0% |
| Nitrogen content | 11.5-12.8% | 11.5-12.8% |

## 10. Typical Properties

*Acidity/alkalinity*:
pH = 3.0-7.0 (5% w/v aqueous solution)
*Compressibility*: *see* HPE Data.
*Density*: 1.17-1.18 g/cm$^3$

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R&D/QC Product Data Sheet Approved By:
~~21 MAR 2006~~
Part Number: PN 10004 Date ~~21 MAR 30~~ OCT 09
R&D: 21 MAR 01
QC: 21 NOV 00

**PLASDONE K-29/32**

**SALES SPECIFICATIONS**

**Chemical Description:**

Polymer of 1-vinyl-2-pyrrolidone. Pharmaceutical Grade K-29/32

**Specifications:**

| | |
|---|---|
| Appearance @ 25 deg. C | White to creamy white powder |
| Identification Tests (Q237 & W1125) | Meets all ID tests |
| Appearance @ 25 deg. C (5% as is aqueous soln., TC200135) | Free of haze |
| + European Color Test – B Color (W731) | B6 Minimum |
| + European Color Test – BY Color(W731) | BY6 Minimum |
| + European Color Test – R Color (W731) | R6 Minimum |
| % Moisture (Karl Fischer, W623) | 5.0 Maximum |
| pH (5% as is aqueous solution, Q231) | 3.0 - 5.0 |
| % Ash (Residue on ignition or Sulphated, W720) | 0.02 Maximum |
| ppm Vinyl Pyrrolidone (HPLC, W686) | 5.0 Maximum |
| % 2-pyrrolidone (W1406) | 3.0 Maximum |
| ppm Heavy Metals (as Lead, W719) | 5 Maximum |
| % Aldehydes (Calculated as acetaldehyde, W652) | 0.05 Maximum |

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## PLASDONE K-29/32

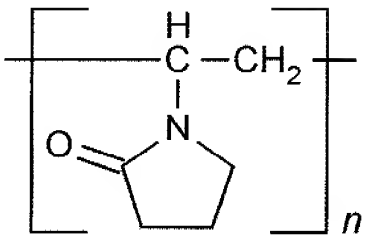
## SALES SPECIFICATIONS

| | |
|---|---|
| % Nitrogen (Solids Basis, W1118) | 12.0 – 12.8 |
| K-Value (Viscosity of 1% solids w/v aqueous solution, W625) | 29 – 32 |
| ppm Peroxide Content (Titanyl Sulfate Method, W028) | 400 Maximum |
| ppm Hydrazine (W403) | 1.0 |
| Total Aerobic Plate Count, CFU/g (Q200) | 100 Maximum |
| Mold/Yeast, CFU/g (Q200) | 100 Maximum |
| Staphylococcus Aureus CFU/g (Q200) | Negative |
| Salmonella, CFU/g (Q200) | Negative |
| Pseudomonas aeruginosa, CFU/g (Q200) | Negative |
| E. coli, CFU/g (Q200) | Negative |

+ B, BY or R color must be 6 minimum. Use appearance solution

Material meets the requirements for Povidone in current US, European and Japanese Pharmacopeias.

**Povidone**



$(C_6H_9NO)_n$

2-Pyrrolidinone, 1-ethenyl-, homopolymer.
1-Vinyl-2-pyrrolidinone polymer [*9003-39-8*].

» Povidone is a synthetic polymer consisting essentially of linear 1-vinyl-2-pyrrolidinone groups, the degree of polymerization of which results in polymers of various molecular weights. The different types of Povidone are characterized by their viscosity in aqueous solution, relative to that of water, expressed as a K-value. (See the section on *K-value* below.) The K-value of Povidone having a stated (nominal) K-value of 15 or less is not less than 85.0 percent and not more than 115.0 percent of the stated values. The K-value of Povidone having a stated K-value or a stated K-value range with an average of more than 15 is not less than 90.0 percent and not more than 108.0 percent of the stated value or of the average of the stated range.

**Packaging and storage—** Preserve in tight containers.

**Labeling—** Label it to state, as part of the official title, the K-value or K-value range of the Povidone .

**Identification—**

**A:** To 10 mL of a solution (1 in 50) add 20 mL of 1 N hydrochloric acid and 5 mL of potassium dichromate TS: an orange-yellow precipitate is formed.

**B:** Dissolve 75 mg of cobalt nitrate and 300 mg of ammonium thiocyanate in 2 mL of water. To this solution add 5 mL of a solution of Povidone (1 in 50), and render the resulting solution acid by the addition of 3 N hydrochloric acid: a pale blue precipitate is formed.

**C:** To 5 mL of a solution (1 in 200) add a few drops of iodine TS: a deep red color is produced.

**pH** ⟨ 791 ⟩ **:** between 3.0 and 7.0, in a solution (1 in 20).

**Water,** *Method I* ⟨ 921 ⟩ **:** not more than 5.0%.

**Residue on ignition** ⟨ 281 ⟩ **:** not more than 0.1%.

**Lead** ⟨ 251 ⟩ — Dissolve 1.0 g in 25 mL of water: the limit is 10 ppm.

**Limit of aldehydes—**

*Phosphate buffer*— Transfer 8.3 g of potassium pyrophosphate to a 500-mL volumetric flask, and dissolve in 400 mL of water. Adjust, if necessary, with 1 N hydrochloric acid to a pH of 9.0, dilute with water to volume, and mix.

*Aldehyde dehydrogenase solution*— Transfer a quantity of lyophilized aldehyde dehydrogenase equivalent to 70 units to a glass vial, dissolve in 10.0 mL of water, and mix. [ NOTE— This solution is stable for 8 hours at 4°. ]

*NAD solution*— Transfer 40 mg of nicotinamide adenine dinucleotide to a glass vial, dissolve in 10.0 mL of *Phosphate buffer,* and mix. [ NOTE— This solution is stable for 4 weeks at 4°. ]

*Standard preparation*— Add about 2 mL of water to a glass weighing bottle, and weigh accurately. Add about 100 mg (about 0.13 mL) of freshly distilled acetaldehyde, and weigh accurately. Transfer this solution to a 100-mL volumetric flask. Rinse the weighing bottle with several portions of water, transferring each rinsing to the 100-mL volumetric flask. Dilute the solution in the 100-mL volumetric flask with water to volume, and mix. Store at 4° for about 20 hours. Pipet 1 mL of this solution into a 100-mL volumetric flask, dilute with water to volume, and mix.

*Test preparation*— Transfer about 2 g of Povidone , accurately weighed, to a 100-mL volumetric flask, dissolve in 50 mL of *Phosphate buffer,* dilute with *Phosphate buffer* to volume, and mix. Insert a stopper into the flask, heat at 60° for 1 hour, and cool to room temperature.

*Procedure*— Pipet 0.5 mL each of the *Standard preparation,* the *Test preparation,* and water to provide the reagent blank into separate 1-cm cells. Add 2.5 mL of *Phosphate buffer* and 0.2 mL of *NAD solution* to each cell. Cover the cells to exclude oxygen. Mix by inversion, and allow to stand for 2 to 3 minutes at 22 ± 2°. Determine the absorbances of the solutions at a wavelength of 340 nm, using water as the reference. Add 0.05 mL of *Aldehyde dehydrogenase solution* to each cell. Cover the cells to exclude oxygen. Mix by inversion, and allow to stand for 5 minutes at 22 ± 2°. Determine the absorbances of the solutions at a wavelength of 340 nm, using water as the reference. Calculate the percentage of aldehydes, expressed as acetaldehyde, in the Povidone taken by the formula:

$$100(C/W)\left[\frac{(A_{U2}-A_{U1})-(A_{B2}-A_{B1})}{(A_{S2}-A_{S1})-(A_{B2}-A_{B1})}\right],$$

in which $C$ is the concentration, in mg per mL, of acetaldehyde in the *Standard preparation; W* is the weight, in g, of Povidone taken; $A_{U1}$, $A_{S1}$, and $A_{B1}$ are the absorbances of the solutions obtained from the *Test preparation, Standard preparation,* and water reagent blank, respectively, before addition of the *Aldehyde dehydrogenase solution;* and $A_{U2}$, $A_{S2}$, and $A_{B2}$ are the absorbances of the solutions obtained from the *Test preparation, Standard preparation,* and water reagent blank, respectively, after addition of the *Aldehyde dehydrogenase solution:* not more than 0.05% is found.

**Limit of hydrazine**— Transfer 2.5 g to a 50-mL centrifuge tube, add 25 mL of water, and mix to dissolve. Add 500 µL of a 1 in 20 solution of salicylaldehyde in methanol, swirl, and heat in a water bath at 60° for 15 minutes. Allow to cool, add 2.0 mL of toluene, insert a stopper in the tube, shake vigorously for 2 minutes, and centrifuge. Apply 10 µL of the clear upper toluene layer in the centrifuge tube and 10 µL of a Standard solution of salicylaldazine in toluene containing 9.38 µg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨ 621 ⟩) coated with a 0.25-mm layer of dimethylsilanized chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of methanol and water (2:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by examination under UV light at a wavelength of 365 nm: salicylaldazine appears as a fluorescent spot having an $R_F$ value of about 0.3, and the fluorescence of any salicylaldazine spot from the test specimen is not more intense than that produced by the spot obtained from the Standard solution (1 ppm of hydrazine).

**Vinylpyrrolidinone—**

*Mobile phase*— Prepare a mixture of water and methanol (80:20).

*Resolution solution*— Transfer 10 mg of vinylpyrrolidinone and 500 mg of vinyl acetate, accurately weighed, to a 100-mL volumetric flask, and dissolve in and dilute with methanol to volume. Transfer 1.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

*Standard solution*— Transfer an accurately weighed quantity of 50 mg of vinylpyrrolidinone to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 1.0-mL of this solution to a 100-mL volumetric flask, dilute with methanol to volume, and mix. Transfer 5.0 mL of this solution to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

*Test solution*— Transfer an accurately weighed quantity of about 250 mg of Povidone to a 10-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

*Chromatographic system* (see *Chromatography* ⟨ 621 ⟩)— The liquid chromatograph is equipped with a 235-nm detector, a 4.0-mm × 2.5-cm guard column containing packing L7, and a 4.0-mm × 25-cm analytical column containing 5-µm packing L7. [ NOTE— The analysis can also be performed with a 4.0-mm × 30-mm or a 4.6-mm × 30-mm guard column containing packing L7 and with a 4.6-mm × 25-cm analytical column containing 5-µm packing L7. ] The column temperature is maintained at about 40°. Adjust the flow rate so that the retention time of vinylpyrrolidinone is about 10 minutes. Chromatograph the *Resolution solution,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between vinylpyrrolidinone and vinyl acetate is not less than 2.0. Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections is not more than 2.0%.

*Procedure*— Separately inject equal volumes (about 50 µL) each of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the responses for the vinylpyrrolidinone peak. [ NOTE— If necessary, after each injection of the *Test solution,* wash the polymeric

material of Povidone from the guard column by passing the *Mobile phase* through the column backwards for about 30 minutes at the same flow rate. ] Calculate the percentage of vinylpyrrolidinone in the sample taken by the formula:

$$1000(C/W)(r_U/r_S)$$

in which $C$ is the concentration, in mg per mL, of vinylpyrrolidinone in the *Standard solution; W* is the weight, in mg, of Povidone taken to prepare the *Test solution;* and $r_U$ and $r_S$ are the peak responses for vinylpyrrolidinone obtained from the *Test solution* and *Standard solution,* respectively: not more than 0.001% is found.

**K-value—** Accurately weigh a quantity of undried Povidone equivalent on the anhydrous basis to the amount specified in the following table:

| Nominal K-value | g |
|---|---|
| ≤18 | 5.00 |
| >18 to ≤95 | 1.00 |
| >95 | 0.10 |

Dissolve it in about 50 mL of water in a 100-mL volumetric flask, dilute with water to volume, and mix. Allow to stand for 1 hour. Determine the viscosity, using a capillary-tube viscosimeter (see *Viscosity* ⟨ 911 ⟩), of this solution at 25 ± 0.2°. Calculate the K-value of Povidone by the formula:

$$[\sqrt{300c \log z + (c + 1.5c \log z)^2} + 1.5c \log z - c]/(0.15c + 0.003c^2),$$

in which $c$ is the weight, in g, on the anhydrous basis, of the specimen tested in each 100.0 mL of solution; and $z$ is the viscosity of the test solution relative to that of water.

**Nitrogen content—** Proceed as directed under *Nitrogen Determination, Method II* ⟨ 461 ⟩, using about 0.1 g of Povidone, accurately weighed. In the procedure, omit the use of hydrogen peroxide, use 5 g of a powdered mixture of potassium sulfate, cupric sulfate, and titanium dioxide (33:1:1), instead of potassium sulfate and cupric sulfate (10:1), and heat until a clear, light-green solution is obtained, then heat for a further 45 minutes: the nitrogen content, on the anhydrous basis, is not less than 11.5% and not more than 12.8%.

**Auxiliary Information—** *Staff Liaison*: Kevin T. Moore, Ph.D., Scientist
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*USP31–NF26* Page 3048
*Pharmacopeial Forum*: Volume No. 30(4) Page 1292
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